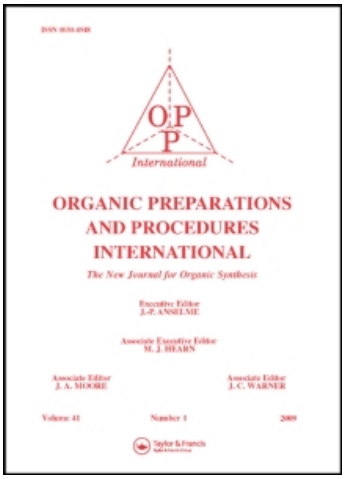

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ALKYLATION OF PHENYLACETONITRILE USING POTASSIUM CARBONATE AS A BASE†

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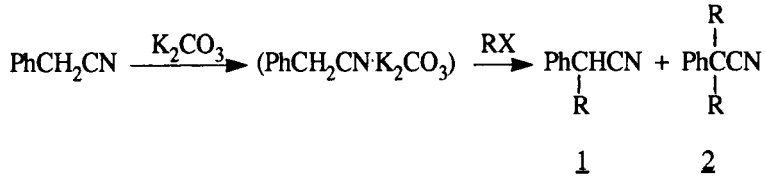
We have reported that compounds having an active methylene group, such as diethyl malonate, ethyl cyanoacetate,[1] acetylacetone,[2] ethyl acetoacetate,[3] can be alkylated simply by heating the substrate and alkyl halide with potassium carbonate in absence of catalyst and solvent; we have also shown that an intermediate potassium carbonate complex is formed during the reaction. We now report that the extremely weak carbon acid, phenylacetonitrile, can also be alkylated in similar fashion. Phenylacetonitrile does not react with alkyl halides and neither does potassium carbonate with most simple normal alkyl halides. Nevertheless, phenylacetonitrile can react with halides in the presence of potasium carbonate. An intermediate complex seems to be formed during reaction as was observed during alkylation of acetylacetone.[2]



a) R = CH_3-; b) R = RCH_3CH_2-; c) R = $CH_3(CH_2)_2$-; d) R = $CH_3(CH_2)_3$-;
e) R = $CH_3(CH_2)_4$-; f) RR = -$(CH_2)_4$-; g) R = -CH_2CO_2Et

The conversions of phenylacetonitrile reach 70, 90 and 95% when the molar ratios of phenylacetonitrile to potassium carbonate are 1:1, 1:1.5 and 1:2 respectively. Most of the alkylation occurs within the first ten hours and monoalkylation is at its maximum after 20-25 hours. Further heating increases dialkylation at the expense of the monoalkylation, although dialkylation begins before monoalkylation attains its maximum conversions. Dialkylation decreases as the alkyl halide becomes larger; amyl halides give no dialkylation product. With sodium carbonate, no reaction occurred.

Since secondary alkyl halides undergo elimination and ethyl chloroacetate decomposes in the presence of potassium carbonate at high temperatures, these halides required a lower temperature, as well as longer reaction times. Tertiary alkyl halides did not give any alkylated products even at lower temperature since they readily undergo elimination. 1,4-Dichlorobutane afforded a 75% yield of 1-phenyl-1-cyanocyclopentane. n-Butyl chloride did not react under our experimental conditions. The lower boiling alkyl halides should be added dropwise in order to maintain a sufficiently high reaction temperature, and the quantity of alkyl halide to be used was determined by gas chromatography; an excess of the easily decomposed and low boiling (bp <100°) halides is required.

EXPERIMENTAL SECTION

Pure products for preparing standard charts of gas chromatography were obtained by repeated vacuum distillation or by known methods,[4,5] and were identified by MS, IR and NMR spectra recorded on JEOL D300S, Perkin-Elmer 783, and EM 360 instruments, respectively. The IR spectra were measured neat on NaCl plates. The proton NMR spectra were determined in CCl_4 with TMS as an external standard.

TABLE. Alkylation of Phenylacetonitrile[a]

RX	Temp (°C)	Conversion (%) at Maximum Monoalkylation[b]			Conversion (%) at End of Reaction			Yield (%)		
		time (hrs)	1	2	time (hrs)	1	2	1	2	SM
EtBr	180 ±5	25	80	15	55	73	21	58	16	4
EtI	180 ±5	25	83	9	44	78	17	58	13	3
PrBr	180 ±5	22	85	5	39	81	18	54	11	2
PrI	180 ±5	17	89	4	43	85	9	63	10	3
iso-PrBr	180 ±5	—	—	—	60	84	—	50	—	17
BuBr	180-190	26	95	1	45	89	4	68	3	16
sec-BuBr	140-183	—	—	—	32	15	—	14	—	13
n-AmBr	187-220	—	—	—	46	83	—	74	—	13
$Ci(CH_2)_4Cl$[d]	177-205	—	—	—	17	—	79[d]	—	75	17
$ClCH_2CO_2Et$[e]	140 ±5	—	—	—	13	30	—	20	—	64

a) SM (starting material) denotes phenylacetonitrile. b) Conversion in liquid layer, calculated on relative mole percentage. c) Total yield of distillation fractions, determined by gas chromatography. d) The product was 1-phenyl-1-cyanocyclopentane. e) $ClCH_2CO_2Et$ was partially decomposed by potassium carbonate during reaction.

General Procedure.- Powered anhydrous potassium carbonate 10 g (0.144 mol) and phenylacetonitrile 8.4 g (0.072 mol) were placed in a 25 ml 3-necked round bottom flask, equipped

with a thermometer and a pressure-equalizing addition funnel containing the alkyl halide. A reflux condenser was connected to the upper neck of the addition funnel to condense vaporized halide and water. The third neck of the flask was stoppered with a glass stopper and used for sampling. The flask was heated in an oil bath. The alkyl halide was added dropwise while the reaction temperature was kept within the desired range (see Table). The water produced vaporized and condensed with the alkyl halide into the funnel. The reaction was continued until carbon dioxide no longer evolved. After cooling, water was added to dissolve the inorganic salts. The oily layer was separated and fractionally distilled under reduced pressure, and the fractions were identified and determined by gas chromatography.

α-Phenylpropionitrile (1a): bp. 85-87°/4 mm Hg, lit.[7,4,6] 112°/16, 112-114°/13, 90-91°/5.5. MS: m/e 131, 116 (base); NMR: δ 1.50 (3 H, d, J = 7 Hz, CH_3) 3.80 (1 H, q, J = Hz, CH) 3.80 (1 H, q, J = 7.0 Hz, CH) 7.37 (5 H, s, C_6H_5); IR: 3055, 3021, 2978, 2930, 2870, 2237, 1597, 1490s, 1450s, 1375 cm^{-1}.

α-Methyl-α-phenylpropionitrile (2a): bp. 83-86°/2 mm Hg, lit.[7] 114-116°/14. MS: m/e 145, 131, 116 (base); NMR: δ 1.67 (6 H, s, $2CH_3$) 7.47 (5 H, quint, J = 4.0 Hz, C_6H_5); IR: 3080, 3055, 2975s, 2931, 2865, 2235s, 1740vs, 1600s, 1492s, 1451s, 1390, 1358s, 1237vs, 1096, 1060, 1030s, 762vs, 700vs cm^{-1}.

α-Phenylbutyronitrile (1b): bp. 101-102°/6 mm Hg, lit.[4,8] 109-110°/10, 102-104°/7. MS: m/e 145, 117; NMR: δ 0.93 (3 H, t, J = 7.0 Hz, CH_3) 1.76 (2 H, quint, J = 7.0 Hz, CH_2) 3.64 (1 H, t, J = 7.0 Hz, CH) 7.28 (5 H, s, C_6H_5); IR: 3320b, 3060, 3025, 2965s, 2930s, 2875s, 2235s, 1720w, 1600m, 1490vs, 1380s, 1090m, 1080, 1070m, 1030m, 760vs, 700vs cm^{-1}.

α-Propyl-α-phenylvaleronitrile (2c): bp. 122-134°/4 mm Hg, lit.[9] 142.5-145°/15. MS: m/e 201, 159, 129, 116, 97, 43 (base); NMR: δ 0.88 (6 H, t, J = 4.0 Hz, $2CH_3$) 1.03-2.03 (8 H, m, 4 CH_2) 7.24 (5 H, s, C_6H_5); IR: 3440b, 3059w, 3025w, 2957s, 2930s, 2868s, 2230, 1742vs, 1599w, 1491, 1461,14446s, 1369s, 1232vs, 1162, 1092, 1068, 1048, 1028, 1020, 762s, 699vs cm^{-1}.

α-Phenylhexanenitrile (1d): bp. 114-116°/1 mm Hg, lit.[7] 107°/2. MS: m/e 173, 145, 117, 105 (base); NMR: δ 0.8 (3 H, t, J = 2.0 Hz, CH_3) 1.27 (4 H, m, 2 CH_2) 1.65 (2H, t, J = 7.0 Hz, CH_2) 3.53 (1H, t, J = 7.0 Hz, CH) 7.17 (5 H, s, C_6H_5); IR: 3082w, 3050w, 2022w, 2952s, 2857s, 2235, 1730m, 1683m, 1598m, 1490s, 1462s, 1452s, 1377w, 753s, 699vs cm^{-1}.

α-Phenylheptanenitrile (1e): bp. 118-121°/1 mm Hg, lit.[7] 112°/1.5. MS: m/e 187, 159, 117, 103, 91, 43 (base); NMR: δ 0.70 (3 H, t, CH_3) 1.0-1.90 (8 H, m, 4 CH_2) 3.47 (1 H, t, J = 7.0 Hz, CH) 7.10 (5 H, quint, J = 14 Hz, C_6H_5); IR: 3055w, 3025w, 2949vs, 2922vs, 2855s, 2235m, 1599w, 1491m, 1450, 1377, 752s, 697vs cm^{-1}.

1-Phenyl-1-cyanocyclopentane (2f): bp. 137°/12 mm Hg, lit.[12] 110°/2. MS: m/e 171, 143, 129 (base), 115, 102, 91; NMR: δ 1.8-2.6 (8 H, m, 4 CH_2) 7.45 (5H, quint, J = 2.0 Hz, C_6H_5); IR: 3062w, 3030w, 2970s, 2880m, 2249m, 1810, 1611m, 1509s, 1467s, 1326w, 1046m, 780vs, 726vs cm^{-1}.

Ethyl β-Cyano-β-phenylpropionate (1g): bp. 150°/4 mm Hg, lit.[11] 156°/7. MS: m/e 203, 175, 158, 129 (base), 116, 103, 91, 77; NMR: δ 1.12 (3 H, t, J = 7.0 Hz, CH_3) 2.73 (1 H, 2d, J = 3.0 Hz, CH) 3.8-4.3 (4H, m, CH_2) 7.2 (5 H, s, C_6H_5); IR: 3440b, 3060w, 2980m, 2932w, 2240m, 1733vs, 1599w, 1494w, 1450m, 1370s, 1347m,1251s, 1206s, 1188vs, 1163s, 1020m, 757s, 698vs cm^{-1}.

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